

That which is claimed is:

1. A method for treating diabetes mellitus, said method comprising contacting a biological system with an effective amount of a compound which inhibits binding of CREB to CBP.

5 2. A method according to claim 1 wherein said treatment of diabetes mellitus ameliorates hyperglycemia.

3. A method according to claim 2 wherein gluconeogenesis is modulated.

4. A method according to claim 3 wherein
10 transcription of PEPCK is inhibited.

5. A method according to claim 2 wherein transcription of glucogen gene is inhibited.

~~6. A method according to claim 1 wherein said biological system is an intact organism.~~

15 7. A method according to claim 1 wherein said contacting is carried out by oral, intravenous, subcutaneous, intramuscular or intracutaneous mode of administration.

20 8. A method for identification of a compound which inhibits activation of cAMP and mitogen responsive genes, said method comprising:

(a) contacting a modified host cell with a test compound, wherein said modified host cell comprises:

25 a first fusion protein comprising a GAL4 DNA binding domain, operatively associated with the KID domain of CREB,

30

a second fusion protein comprising an activation domain, operatively associated with the KIX domain of CBP, and

a reporter construct comprising a GAL4 response element operatively linked to a reporter gene; and

35

- (b) selecting those test compounds which cause reduced expression of the reporter gene product.

9. A method according to claim 8, wherein said GAL4 DNA binding domain is operatively associated with CREB.

10. A method according to claim 8, wherein said activation domain is operatively associated with CBP.

11. A method according to claim 8 wherein compounds which disrupt complex comprising CREB and CBP are identified.

12. A method for treating diabetes mellitus, comprising contacting a biological system with an effective amount of a compound identified by the method of claim 8.

13. A method to identify compounds which disrupt complex comprising CREB and CBP, said method comprising:

5

- (a) contacting a modified host cell with a test compound, wherein said modified host cell comprises:

a first fusion protein comprising an activation domain, operatively associated with the KID domain of CREB,

10

a second fusion protein comprising a GAL4 DNA binding domain, operatively associated with the KIX domain of CBP, and

15

a reporter construct comprising a GAL4 response element operatively linked to a reporter gene; and

- (b) selecting those test compounds which cause reduced expression of the reporter gene product.

20

14. A method according to claim 13, wherein said activation domain is operatively associated with CBP.

15. A method according to claim 13, wherein said GAL4 DNA binding domain is operatively associated with CBP.

25

16. A method according to claim 13 wherein compounds which disrupt complex comprising CREB and CBP are identified.

17. A method for treating diabetes mellitus, comprising contacting a biological system with an effective amount of a compound identified by the method of claim 13.

Sub. GI
add E3
add F6